Recommendations and cardiological evaluation of athletes with arrhythmias Part 1

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Besides the consensus meeting in Amersfoort in 1988 and the Bethesda conference in 1994 recommendations are not available in the Netherlands for screening and evaluation of athletes with cardiac arrhythmias.[1,2]

Guidelines for competitive athletes with cardiac arrhythmias in the United States and Italy were published in 2000.[2,3] In 1998 Estes et al.[4] published the most important opinions on sudden cardiac death, screening and evaluation of athletes and arrhythmias.

This study addresses the physiological and morphological consequences of athletic training, cardiac pathology and risk stratification for sudden cardiac death. Recommendations for competitive athletes with cardiovascular abnormalities, arrhythmias and proposals for specific protocols are given. (*Neth Heart J* 2004;12:157-64.)

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Cardiac adaptations and morphological consequences of athletic performance

Increased levels in maximal oxygen intake ($VO_{2\,max}$), increased maximal cardiac output, increased widening of maximal arteriovenous oxygen content difference, increase in stroke volume and a decrease in resting heart rate are the physiological cardiovascular effects of systematic training. The combination of these features is called 'the athletic heart syndrome'.[5,6]

The morphological cardiovascular consequence of systematic training in athletes is dependent on the type and intensity of the training schedule, gender and age of the athlete. The combination of isotonic and isometric exercise will give a wide spectrum of cardiovascular adaptations.

The isotonic or dynamic stress is associated with volume loading of the myocardium and leads to eccentric left ventricular hypertrophy. Ventricular mass and dimension are found to have increased in endurance athletes, usually by 35 to 45%. Isometric or static stress is associated with a pressure loading of the left ventricle and could lead to disproportionate increase in wall thickness. In table 1 a summary of the pure form of adaptation is given.

Table 2 shows the classification of sports based on isotonic and isometric components during different sporting activities.

The ECG of an athlete can show aberrations in a broad spectrum. Endurance training for a long period of time induces changes in heart rate, conduction and repolarisation. The most striking changes are bradycardia and large voltages of the QRS complex, suggestive of left ventricular hypertrophy. As regards to the repolarisation pattern of an athlete's ECG, it is difficult to differentiate between structural heart disease and a normal heart.

In a large study by Pellicia et al.[7] 5% of the athletes had structural heart disease and 51% of them had an abnormal ECG. Forty-nine percent of the athletes with structural heart disease had a normal ECG. Of the 952 athletes without evidence of cardiac disease, 375 (39%)

Table 1. Physiological and morphological cardiac adaptation to systematic training.

Isotonic loading
- Increased stroke volume and end-diastolic volume
- Increased $VO_{2\,max}$
- Increased aerobic power (respiration) of the skeletal muscle
- Cardiac mass-volume ratio unchanged

Isometric loading:
- Increased left ventricular mass
- No increase in $VO_{2\,max}$
- No increase in LVED
- Increase in cardiac mass-volume ratio

LVED=left ventricular end-diastolic dimension.

had an abnormal ECG and could be classified as false-positives.

Nontraumatic sudden death in athletes

The benefit of physical training in preventing cardiovascular disease has been subject of many studies.[8,9] Sudden cardiac death in athletes is a rare, an unexpected and emotional event. Sudden cardiac death is defined here as the abrupt, unexpected death of cardiovascular aetiology, in which there is loss of consciousness within one hour of onset of symptoms.[10]

The incidence of sudden cardiac death in the general population is three to ten cases per 10,000 subjects,[4] 90% of the victims are male.[11] In the Netherlands the incidence is between 150 and 200 athletes/year.[12] Analysis of postmortem studies shows a similar entity of cardiac diagnosis,[13] which can precipitate sudden cardiac death in male athletes. There is a difference in the causes of sudden and nonsudden death in men (including athletes) related to age. The risk of sudden death in the group of men, including athletes, younger than 35 is 0.5 to 1 per 100,000/year. Males older than 35 years clearly show a higher mortality at 1 to 2 per 1000/year.[4]

In the group under 35 years of age, hypertrophic cardiomyopathy is responsible for 40% of sudden deaths, the second most frequent cause is a coronary anomaly in which the coronary artery is located between the aorta and the pulmonary artery (figure 1). The remaining other diseases, idiopathic myocardial hypertrophy, arrhythmogenic right ventricular dysplasia (ARVD), Wolff-Parkinson-White Syndrome with a bypass tract with a short refractory period, long-QT syndrome, myocarditis, Marfan's syndrome and premature coronary artery disease are depicted in tables

Table 2. Classification of sports.[2]

Classification of sports	A. Low isotonic	B. Moderate isotonic	C. High isotonic
I. Low isometric	Billiards	Baseball	Badminton
	Bowling	Softball	Cross-country skiing
	Cricket	Table tennis	Field hockey
	Golf	Tennis doubles	Race walking
	Riflery	Volley-ball	Running
		Soccer	
		Squash	
		Tennis singles	
II. Moderate isometric	Archery	Fencing	Basketball
	Auto racing	Figure skating	Ice hockey
	Diving	Rugby	Cross-country skating
	Equestrian	Running sprint	Running middle distance
	Motorcycling	Surfing	Team handball
III. High isometric	Bobsledding	Body building	Boxing
	Gymnastics	Downhill skiing	Canoeing/Kayaking
	Karate/Judo	Swimming	Cycling
	Sailing	Wrestling	Decathlon
	Rock-climbing	Water polo	Rowing
	Water-skiing		Speed skating
	Weight-lifting		
	Windsurfing		

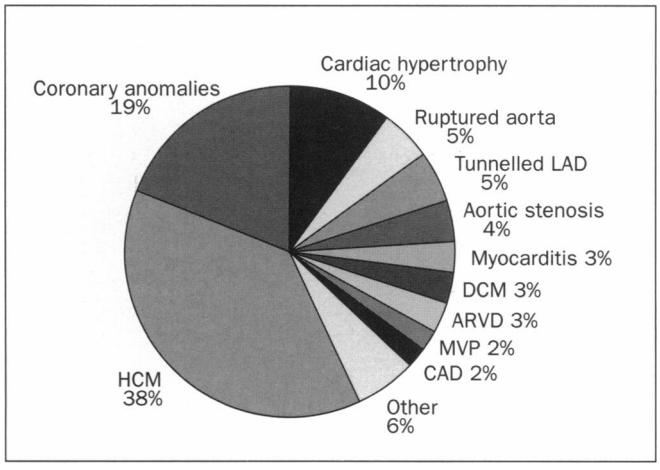

Figure 1. Estimated prevalence of sudden cardiac death in athletes younger than 35.

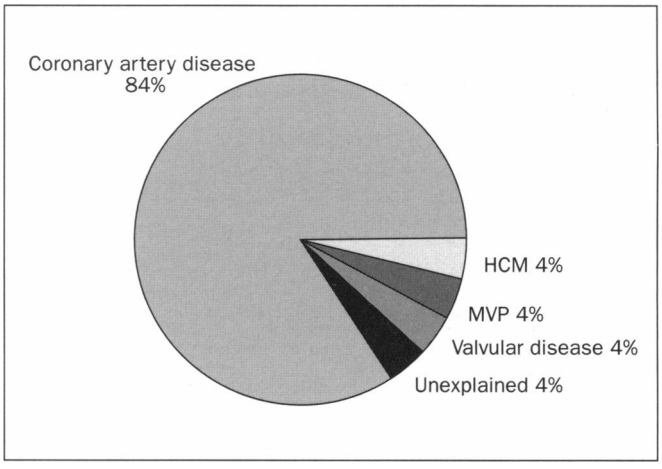

Figure 2. Estimated prevalence of sudden death in athletes older than 35.

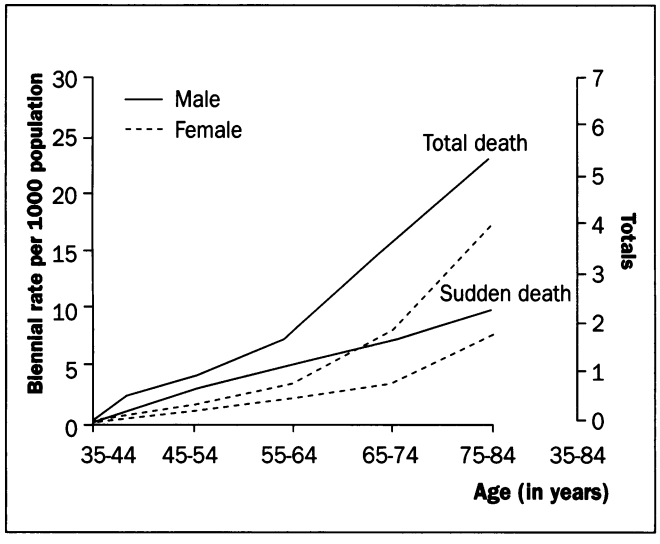

Figure 3. Sex- and age-specific rates for sudden cardiac death and total coronary heart disease deaths.[26]

Table 3. Prevalence of cardiovascular disease and risk for sudden death in the UK.[18]

Diagnosis	Prevalence	Persons at risk
HCM	20:10,000	100,000
ARVD	1:10,000	5000
WPW	15:10,000	75,000
LQTS	1:10,000	5000
CAA	20:10,000	100,000
MVP	200:10,000	1,000,000
Marfan	2:10,000	10,000

HCM=hypertrophic cardiomyopathy, ARVD=arrhythmogenic right ventricular cardiomyopathy, WPW=Wolff-Parkinson-White syndrome, LQTS=long-QT syndrome, CAA=congenital coronary artery anomaly, MVP=mitral valve prolapse.

3 and 4. In the group over 35 years of age an acute coronary syndrome is responsible for more than 80% of sudden cardiac deaths. Less frequent causes are hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM), ARVD, mitral valve prolapse (MVP) and valve disease (figure 2.)

Gender-related differences

Differences are found between men and women in ECG, QT interval, mean heart rate and dimension of the ventricle. The QT interval in women is more prolonged at low heart rates than in men and this is associated with the finding that ventricular arrhythmia, such as torsade de pointes, is more common in women. The highest quartile of the prolonged QTc interval in women is associated with an increased risk factor for cardiac mortality.[14] A 26-year follow-up in the

Table 4. Cardiac and noncardiac causes of sudden cardiac death.[17]

Cardiac causes	Noncardiac causes?
HCM	Arteriovenous anomaly
CAD	WPW
ARVD	Myocardial bridging
CAA	Coronary aneurysm
LVH	Subvalvular aortic stenoses
Myocarditis	LQTS
Conduction disorder	Idiopathic VF
Mitral valve prolapse	DCM
Valve disease	Cerebral embolus
Aorta dissection	Pulmonary embolus

HCM=hypertrophic cardiomyopathy, CAD=coronary artery disease, ARVD=arrhythmic right ventricular cardiomyopathy, CAA=congenital coronary artery anomalies, LVH=left ventricular hypertrophy, WPW=Wolff-Parkinson-White syndrome, LQTS=long-QT syndrome, VF=ventricular fibrillation, DCM=dilated cardiopathy.

Table 5. Diagnostic criteria for right ventricular dysplasia.[11]

I. Global and/or regional dysfunction and structural alterations
Major:
- Severe dilatation and reduction of RV ejection fraction with no (or only mild) LV impairment
- Localised RV aneurysms (akinetic or dyskinetic areas with diastolic bulging)
- Severe segmental dilatation of the RV

Minor:
- Mild global RV dilatation and/or ejection fraction reduction with normal LV
- Mild segmental dilatation of the RV
- Regional RV hypokinesia

II. Endomyocardial biopsy findings
Major:
- Fibro-fatty replacement of myocardium

III. Repolarisation abnormalities
Minor:
- Inverted T waves in right precordial leads (V_2 and V_3) (if more than 12 years and no right bundle branch block)

IV. Depolarisation/conduction abnormalities
Major:
- Epsilon waves or localised prolongation (>110 ms) of the QRS complex in right precordial leads (V_1-V_3)

Minor:
- Late potentials on signal-averaged ECG

V. Arrhythmias
Minor:
- Left bundle branch block type sustained or nonsustained VT on ECG, Holter or exercise testing
- Frequent ventricular extra systoles (more than 1000/24 hours)

VI. Family history
Major:
- Familial disease confirmed at autopsy or surgery

Minor:
- Familial history of premature sudden death (≤35 years) due to suspected right ventricular dysplasia
- Familial history (clinical diagnosis based on present criteria)

Framingham study shows a clear difference in sudden cardiac death between men and women (figure 3).

Screening athletes at risk of sudden cardiac death

In general it is not advisable to screen large groups of asymptomatic athletes because of the very low incidence of sudden cardiac death. Epstein et al.[15] estimated the value of screening: to identify ten athletes with a significant risk of SCD, 200,000 subjects had to be screened under the age of 30. One out of these, ten subjects at risk will actually suffer SCD.

Nevertheless, several investigators are of the opinion that one could identify subjects at risk with a combination of appropriate history and physical examination focused on the major diseases mentioned in figure 1 and table 4.[13,15-17]

Sharma et al.[18] published a summary of the incidence and prevalence of athletes risking SCD (table 3) and made suggestions for identifying subjects at risk, screening and proper diagnosis.

Prominent cardiac disorders provoking sudden death in competitive sport

1. Hypertrophic cardiomyopathy

Hypertrophic cardiomyopathy is a primary heart muscle disorder with autosomal dominant inheritance,[19] with a prevalence of 2:1000 in the general population. Sudden death is sometimes the first symptom of the disease and the causes are atrial arrhythmias and ventricular tachycardias provoked by exercise. Athletes with HCM run a higher risk of sudden death than non-athletes.[20]

Specific medical history can include young sudden death victims in the family, exertion-related dyspnoea, light-headedness during or shortly after exertion, history of syncope, chest discomfort, palpitations and early fatigue. Abnormalities in physical examination are abnormal jugular venous wave, prominent carotid pulse in case of outflow obstruction. The examination of the athlete should be conducted sitting up and

standing, with auscultation of the systolic ejection murmur during Vasalva and squatting.

Diagnosis is based on family history, symptoms, physical examination, ECG, Doppler echocardiography and genetic counselling.

Recommendation

Athletes with an unequivocal diagnosis of hypertrophic cardiomyopathy should not participate in most competitive sports with the possible exception of low-intensity ones (class 1A). This recommendation includes all athletes with or without symptoms of left ventricular outflow obstruction.

Exclusion criteria are athletes older than 35 years with low-risk factors for sudden death, including absence of ventricular arrhythmias, family history of sudden death, history of syncope or near syncope, outflow tract obstruction less than 50 mmHg, exercised-induced hypotension, moderate to severe mitral regurgitation, enlargement of the left atrium, paroxysmal atrial fibrillation and myocardial perfusion defects.

There should be no participation in competitive sport except for low intensity class 1A sport.[2]

2. Arrhythmogenic right ventricular dysplasia

ARVD is a primary heart muscle disorder often associated with autosomal dominant inheritance.[21-27] It is characterised by fibro-fatty atrophy of the right ventricular myocardium and in some cases of the left ventricle as well. Prevalence is 1:10,000 in the general population, but may be higher because of asymptomatic or less symptomatic individuals. The cause of sudden death is ventricular tachycardia and ventricular fibrillation. The fibro-fatty infiltration in the myocardium is considered the mechanism for a re-entry tachycardia.

Specific medical history consists of palpitations during mental or physical stress, syncope and/or chest pain during exertion and family history of sudden cardiac death. Physical examination is not informative. For the diagnostics see table 5. Myocardial biopsies can sometimes give a false-negative result. Therapy options for ARVD are β-blocker including sotalol, ablation and implantable cardioverter defibrillator (ICD).

Recommendation

See HCM.

3. Congenital coronary artery anomalies

The prevalence is probably 2:1000 in the general population.[28,29] The left main coronary artery originates from the right sinus of Vasalva. The left main passes between the aorta and the pulmonary artery; this results in a slit-like orifice. During exertion the coronary artery is compressed between the aorta and pulmonary artery as a result of the increase in their diameter produced by an increase in cardiac output. Excessive torsion of the coronary artery during exercise may exaggerate the slit-like orifice to be obstructed. The resulting ischaemia is the cause of ventricular arrhythmias. Specific medical history is syncope and/or chest pain during exertion, with dyspnoea disproportional to the amount of exertion. Physical examination is not informative. ECG and nuclear stress testing can be normal but echocardiography, transoesophageal echocardiography, MR imaging, computed tomography (CT) and coronary angiogram could be informative. Therapy involves coronary bypass grafting or re-implantation of the coronary arteries.

Recommendation

Detection of these abnormalities should result in exclusion from all competitive sports. Participation in sports >6 months after surgical correction for individuals without exercised induced ischaemia is permitted.

4a. Premature atherosclerotic coronary artery disease

Prevalence is 4 to 9% in competitive athletes. Sudden death results from a ruptured plaque in a coronary artery. Almost all victims have one-vessel disease with fewer than 50% atherosclerotic lesions.[13,30] There are seldom pre-event symptoms, but there can be a family history of manifestations of premature coronary artery disease and/or hypercholesterolaemia. Physical examination is not informative. The ECG is normal at rest, diagnosis can be made by exercise ECG or nuclear stress testing, echocardiography, radionuclide angiography or left ventricular angiography to assess left ventricular function. Therapy options are β-blockers, calcium antagonists, nitrates, antiplatelet drugs and treatment of cardiovascular risk factors. Smoking and cocaine use should be suspended.

4b. Atherosclerotic coronary artery disease, coronary artery disease, post-coronary bypass graft surgery and post-percutaneous transluminal coronary angioplasty with or without stent

Coronary artery disease is the most frequent cause of exercise-induced sudden cardiac death in adults. The incidence of myocardial infarction, sudden death and cardiac arrest increases with vigorous physical activity. Possible mechanisms include plaque rupture, coronary spasm, decreased coronary flow reserve, catecholamine-induced platelet aggregation, hypertension and increasing shear forces in the coronary artery. Physicians should be aware that athletes may minimise symptoms and that cardiac discomfort is not always classical angina but tightness, heartburn, exercise intolerance, unusual dyspnoea or exercise syncope could be prodromal cardiac symptoms. Physical examination is not informative. ECG and exercise ECG or nuclear stress testing could be normal. Echocardiography, radionuclide angiography or coronary angiography and left ventricular angiography are used to assess left ventricular function. Therapy involves β-blockers, calcium

antagonists, nitrates, antiplatelet drugs and treatment of cardiovascular risk factors. Smoking and cocaine use should be stopped.

Recommendation
Two risk levels are defined.

A. Mildly increased risk
1. Normal or nearly normal resting left ventricular function;
2. Normal exercise tolerance for age. $VO_{2\,max}$:
   >35 ml/kg/min <50 years
   >31 ml/kg/min 50-59 years
   >28 ml/kg/min 60-69 years
   >24 ml/kg/min >70 years
3. Absence of exercise-induced ischaemia;
4. Absence of exercise-induced complex ventricular arrhythmias;
5. Absence of haemodynamically significant stenosis in all major coronary arteries.

B. Substantially increased risk
1. Impaired left ventricular systolic function at rest (EF <50%);
2. Evidence of exercised-induced ischaemia;
3. Evidence of exercised-induced complex ventricular arrhythmias;
4. Haemodynamically significant stenosis in a major coronary artery.

Athletes with mildly increased risk can participate in class IA and IIA sports but should avoid intensely competitive situations. Athletes should be examined annually. Athletes with substantially increased risk are generally restricted to class IA sports. Athletes should be examined every six months.[2]

5. Wolff-Parkinson-White syndrome
Prevalence is 1.5:1000 in the general population with a male/female ratio of 2:1.[31] There is a high risk of atrial fibrillation followed by ventricular fibrillation if there is a short refractory period of the accessory pathway. Atrial fibrillation with minimal RR intervals <250 ms at rest or during exercise indicates an atrioventricular bypass tract with a very short refractory period and is a high risk factor for VF and sudden death. Specific medical history involves unexplained palpitations, presyncope and syncope. Physical examination is not informative. The ECG at rest is in sinus rhythm with a short PR interval and delta wave. If the delta wave disappears with a procainamide infusion or during exercise there is a low risk for malignant ventricular arrhythmias. If the delta wave persists during exercise or in cases of doubt about disappearance of the delta wave, there is an indication for further electrophysiological study. Therapy involves RF catheter ablation.

Recommendation
Athletes without structural heart disease, a history of palpitations, or without tachycardia may participate in all competitive sports. For athletes with tachycardias, the recommendations for supraventricular tachycardia apply. Athletes with episodes of atrial fibrillation whose maximal ventricular rate at rest (without therapy) due to conduction over the accessory pathway is <250 beats/min and who have no episodes of syncope or near syncope and have no structural heart disease appear to be at low risk for SCD and may participate in all competitive sports. Athletes with syncope or near syncope or episodes of atrial flutter or atrial fibrillation whose maximal ventricular rate at rest due to conduction over the accessory pathway exceeds 250 beats/min should be scheduled for ablation and are restricted to class IA sports.
Athletes without symptoms after a successful ablative therapy and with no recurrence of the tachycardia for three to six months have no restrictions for competitive sports.[2]

6. Long-QT syndrome (LQTS)
Prevalence in the general population is 1:5000.[32] There are two rare hereditary disorders with QTc >440 ms. The two clinical phenotypes are the autosomal dominant form, the Romano-Ward syndrome, and the autosomal recessive form, the Jervell and Lange-Nielsen syndrome. Seven genotypes are identified in patients with genetic long QTS, LQT1-7. Type I and II account for more than 90% of the cases. Type I is present in children (40% have symptoms before puberty) and its behaviour

Table 6. Drugs and QT prolongation.

Cardiac	Quinidine, procainamide, disopyramide, sotalol, amiodarone, lidoflazine, mexitilene, flecainide, aprindine, bepredil, dofetilide, propafenone
Antibiotics	Ampicillin, erythromycin, trimethoprim, pentamidine, doxyrubicin, ketoconazole, clarithromycin
Antihistaminic H1-receptor antagonism	Prenyamine, astemizole, terfenadine, dyphenhydramine, ebastine, hydroxyzine
Antimalaria drugs	Chloroquine, hydroxychloroquine
Serotonin inhibitors	Fluoxetine, zimeldine, ketanserine
Other drugs	Tricyclic and tetracyclic antidepressant drugs, fenothiazines, chlorahydrate, terodiline, probucol, indoramine, cisapride, cocaine

Table 7. Classification of hypertension.[2]

	Mild stage 1	Moderate stage 2	Severe stage 3	Very severe stage 4
Adolescent 13-15 years				
Systole	135-139	140-149	150-159	>160
Diastole	85-89	90-94	95-99	>100
Adolescent 16-18 years				
Systole	140-149	150-159	160-179	>180
Diastole	90-94	95-99	100-109	>110
Adult >18 years				
Systole	140-159	160-179	180-209	>210
Diastole	90-99	100-109	110-119	>120

is extremely malignant during exercise. Type II starts at adolescence and in some cases is the first manifestation of SCD at a more advanced age. Some drugs can induce a prolonged QT interval (table 6). The trigger for SCD is torsade de pointes which deteriorates into ventricular fibrillation. The specific medical history involves syncope due to polymorphic ventricular tachycardia and ventricular fibrillation, palpitations, chest complaints and family history. Physical examination is not informative. The ECG shows a prolonged QT interval, 'double hump' in the precordial leads and morphologically abnormal T waves. Defects in chromosome 3, 7 and 11 have specific QT configurations. Echocardiography is normal. The negative Holter monitoring and a negative exercise testing could provide false-negative information. An implantible loop recorder can help to the final diagnosis. Therapy options are β-blocker, pacing or ICD.

Recommendation

There is a restriction for all competitive sports.[2]

7. Myocarditis

The variability in the incidence of myocarditis differs from 1 to 10% in literature.[33] The clinical course in myocarditis is unpredictable. Myocarditis can cause arrhythmias and electrocardiographic changes in athletes. Exercise may predispose to an adverse outcome and could result in sudden cardiac death in the athlete. Specific medical history can include aspecific common cold complaints, light fever, tachycardia and sometimes cardiomegaly. Physical examination reveals a pulsus alternans, gallop and serious left ventricular dysfunction. The ECG shows aspecific repolarisation abnormalities. Abnormal left ventricular function is seen on Doppler.

Recommendations

Restriction from all competitive sports for the 'fever period'. A six-month period is recommended until full convalescence. Athletes with pericarditis are treated according to the same recommendation.[2]

8. Marfan's syndrome

The prevalence of Marfan's syndrome is 1:5000 in the general population.[20,34] Aortic root dilatation predisposes to aortic dissection and rupture resulting in cardiac tamponade and SCD. The medical history is aspecific; family history is positive for Marfan's syndrome. Physical examination reveals ocular manifestations (ectopia lentis) and skeletal abnormalities consisting of dolichostenomalia and shoulder luxations. Diagnostic options are Doppler echocardiography, MR imaging and CT scan. In the case of aorta root dilation of >6 mm prophylactic operation is indicated.[35-37]

Recommendation

Athletes without a family history of premature SCD and without evidence of aortic root dilatation or mitral regurgitation may participate in class IA and IIA sports. Echocardiography should be repeated every six months. Athletes with aortic root dilatation may only participate in class IA sports. Athletes with Marfan's syndrome should not participate in sport with a risk of bodily collision.[2]

9. Mitral valve prolapse (MVP)

Prevalence is 1: 50, one million people in the UK and 15 million in the US.[38] The medical history is aspecific, 90% of the patients with MVP are asymptomatic and 10% have a variable symptomatology. MVP is sometimes associated with WPW and LQTS and Marfan's syndrome. Physical examination reveals the presence of mid-systolic click and a late systolic murmur. Doppler echocardiography is used for diagnosis.

Recommendation

In the absence of symptoms and history of syncope or positive family history of SCD and repetitive forms of (exercised induced) sustained or non-sustained supraventricular or complex ventricular arrhythmias, there is no restriction for competitive sport exists.[2]

10. Hypertension

Hypertension is a risk factor for SCD and ventricular arrhythmia but there is no relation with SCD in young athletes. In 95% of all cases the diagnosis is essential hypertension. Not only the measurement of the blood pressure at rest is important but the dynamic course of the blood pressure during sport-specific exercise has to be recorded as well. Marked increase in systolic blood pressure during exercise (>240 mmHg) is associated with an increased risk of SCD and complex ventricular arrhythmias.[39] For the recommendations no distinction is made between primary or secondary hypertension. For classification of the hypertension by age see table 7.

Recommendation

Athletes with mild and moderate hypertension have no restriction for competitive sport. Athletes with stage 3 and 4 are restricted from class IIIA, IIIB and class IIIC sports.[2] ■

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